One step production of darunavir solid dispersion nanoparticles coated with enteric polymers using electrospraying

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Abstract

Objectives The aim of this work was to investigate the feasibility of producing darunavir (DRV) solid dispersion nanoparticles coated with an enteric polymer in one single step using electrospraying.

Methods The core-shell nanoparticles were made using coaxial electrospraying. A solution of DRV with hydroxypropyl methylcellulose (HPMC) in a mixture of organic solvents formed the core while the shell was produced from an enteric polymer (Eudragit L100) dissolved in an organic solvent. The final particles were evaluated in terms of morphology, physical state, encapsulation efficiency and in vitro dissolution.

Key findings Nanoparticles of encapsulated DRV solid dispersions within Eudragit L100 were successfully prepared with high encapsulation efficiency (90%). The enteric coating layer reduced the percentage of DRV release in acidic medium in the in vitro dissolution test to less than 20%.

Conclusions This study showed the potential of coaxial electrospraying for encapsulating solid dispersions within core-shell structured nanoparticles.

Introduction

Formulation of solid dispersions (SDs) is one of the popular strategies to increase the oral bioavailability of poorly water-soluble drugs. [1] In an ideal SD, namely a glass solution, the active pharmaceutical ingredient (API) is dispersed at a molecular level within a hydrophilic carrier. However, in reality the API molecules very often form amorphous particles/clusters whose physical structure and dimensions depends highly on the preparation method. [2] In general, SDs can be produced by either solvent-based methods (e.g. spray-drying, film casting) or heat-based methods (e.g. hot melt extrusion, spray congealing). [3] The success of preparing a "complete" amorphous glass solution via traditional solvent-evaporation methods relies on a rapid rate of solvent removal. This is challenging because the increase in viscosity during the drying process will hamper further evaporation of the residual solvents. [4] Spray-drying is among the most commonly used processes for SDs preparation. The main advantage of this method is the high efficiency in solvent removal, but downstream/post-processing and stability of the spray-dried products are still challenging. Substantial variations in physicochemical properties of the final dosage forms are often encountered because of the hygroscopic behavior and poor flowability and compressibility of amorphous spray-dried SDs. [5] Moreover, amorphous SDs are physically unstable because they are often supersaturated systems with respect to thermodynamic solid state solubility. [6]

Another challenge in pharmaceutics is coating of the API. An additional layer can be required either to protect unstable APIs in the stomach or to prevent injuries/irritation to the stomach, but also

when a targeted/controlled drug release at a specific site in the gastrointestinal tract is necessary. The coating process is particularly challenging for spray-dried powders consisting of small particles. [7] Kondo el al reported the preparation of sustained-release coated particles by using a three-fluid nozzle spray drying set-up. [8] A crystal suspension and a polymer solution were fed through a central and outer passage of the nozzle, respectively, resulting in the formation of polymer-coated crystalline microparticles. In the present study, we propose electrospraying as a novel process to prepare and coat nanoparticles of solid dispersions in one single step.

Electrospraying can be placed in the group of solvent-based methods. However, it shows an advantage over other traditional solvent-evaporation methods in terms of solvent removal. This technique uses electrical forces to atomize solutions into droplets with diameters in the micro- or nanometer range. [9] The small size of these droplets allows rapid and complete solvent removal. Thus, on the way from the dispensing nozzle to the collector, the produced droplets dry and turn into solid particles. The droplet volume and hence the solid particle size depend on the solution composition and the resulting solution properties as well as the processing parameters. [10] In cases where an API solution is used, because of rapid removal of solvent, one could expect more “complete” amorphous SDs. Both amorphization and nanosizing by electrospraying will contribute to dissolution improvement of poorly water-soluble APIs. However, these are not the only advantages of electrospraying compared to the traditional solvent-based methods. Because of Coulomb repulsion of the charged particles, they are self-dispersing during their flight towards the collector, resulting in less coalescence of the dried particles. [11] Moreover, with an appropriate selection of solutions and process parameters, a narrow particle size distribution may be obtained. This leads to an additional benefit, as monodisperse particles are able to provide more regular and predictable drug release profiles. [12] The nano/micro-particles collected from electrospraying can also be further processed, e.g. as powders for reconstitution, a suitable dosage form for paediatric and elderly patients. This dosage form could offer convenience in terms of use because the administered dose can be easily adapted to the needs of the patients, while the powders comprising nanoparticles can be

reconstituted to a drinkable and milky suspension which leaves no unpleasant and rough feeling in the mouth. Lastly, the electrospraying set-up can be adjusted to produce core-shell particles using nozzles that have two or more channels, so-called coaxial nozzles. Therefore, in this paper, we investigated the feasibility of electrospraying as a one-step process to prepare polymer-coated solid dispersion particles applying a coaxial electrospraying set-up. The resultant particles are core-shell structures with high encapsulation efficiency.

Darunavir (DRV) was used as the poorly water-soluble model drug. Amorphous solid dispersion nanoparticles of DRV with hydroxypropyl methylcellulose (HPMC) were formed and coated simultaneously with Eudragit L100 by using coaxial electrospraying. The rationale for the preparation of coated DRV solid dispersion particles is their use in an advanced fixed dose combination with ritonavir (RTV) as suggested by the WHO. [13] In a previous study, we described how spray-dried ternary solid dispersions of DRV and RTV with HPMC showed a decrease in release of both RTV and DRV compared to binary spray-dried powders of either RTV or DRV, indicating that the simultaneous release of both DRV and RTV from the ternary spray-dried powders has a negative influence on the mutual solubility and the supersaturation behavior of DRV and RTV. [14] Therefore an "advanced" fixed dose combination of DRV and RTV should release RTV separately from DRV. Hence a system that releases RTV in the stomach and DRV later in the small intestine should serve this purpose. In order to achieve this, an enteric coating has to be applied to DRV solid dispersion particles.

Materials and Methods

Materials

Darunavir, in the form of darunavir ethanolate was obtained from Cilag AG (Switzerland). Hydroxypropyl methylcellulose 2910 5mPa.s (HPMC) was provided by Corlocon (UK). Eudragit L100 was obtained from Degussa Rohm GmbH (Germany). Absolute ethanol (EtOH) (AnalaR NORMAPUR®)

and isopropanol (IPA) were obtained from VWR (Belgium). Dichloromethane (DCM) and acetonitrile (HPLC grade) were obtained from Fisher Scientific (Belgium) and Acros Organic (Belgium), respectively. Hydroxypropyl methylcellulose phthalate (HPMCP) (grade 50) and hydroxypropyl methylcellulose acetate succinate (HPMCAS) (grade LF) were obtained from Acros Organic (Belgium). Other chemical reagents were of analytical grade. In all the experiments demineralized water (> 18 MΩ) (Maxima Ultra Pure Water, Elga Ltd, England) was used.

Preparation of encapsulated DRV solid dispersion micro/nanoparticles by coaxial electrospraying

Firstly, preliminary experiments with single-nozzle electrospraying were performed to screen for a suitable enteric polymer (HPMCP, HPMCAS and Eudragit L100) as well as the composition of mixture of organic solvents (DCM, EtOH and IPA) based on their response to different applied voltages. Then the core-shell particles of DRV were prepared by electrospraying using a two-concentric stainless steel nozzle (COAX_2DISP, Linari Engineering, Italy). The coaxial electrospray setup is illustrated in Figure 1. DRV and HPMC were dissolved in a mixture of DCM/IPA/EtOH (2/4/4 v/v/v) to obtain the inner/core solution. A solution of Eudragit L in IPA was used to form the particle shell. The electrospraying was performed in a climate-controlled electrospinning chamber (Electrospinning Apparatus EC-CLI, IME Technologies, the Netherlands) at 25 °C and 50% relative humidity. The solutions were delivered to the nozzles using two syringe pumps (PHD 4400, Harvard Apparatus, Massachusetts, US). The flow rates of the core and the shell solutions were varied and the applied voltage was adjusted accordingly (12-14 kV) to obtain a stable cone-jet mode. Each formulation (different ratio of core/shell flow rates) was prepared in duplicate. The distance between the tip of the nozzle and the collector was fixed at 6 cm. 10 ml of 0.1% (w/v) sodium lauryl sulfate solution in water (pH 4.5) was used as solution collector which was drawn in a homemade receiving dish consisting of an aluminum plate at the bottom and a wall made of Geberit high density polyethylene. At the end of the experiment, a milky suspension was obtained and the micro/nanoparticles

of DRV were isolated from the suspension by freeze-drying at -50°C and 0.04 mBar for 24 hour (Christ Alpha 1-2 LD plus freeze-dryer, SciQuip LTD, UK).

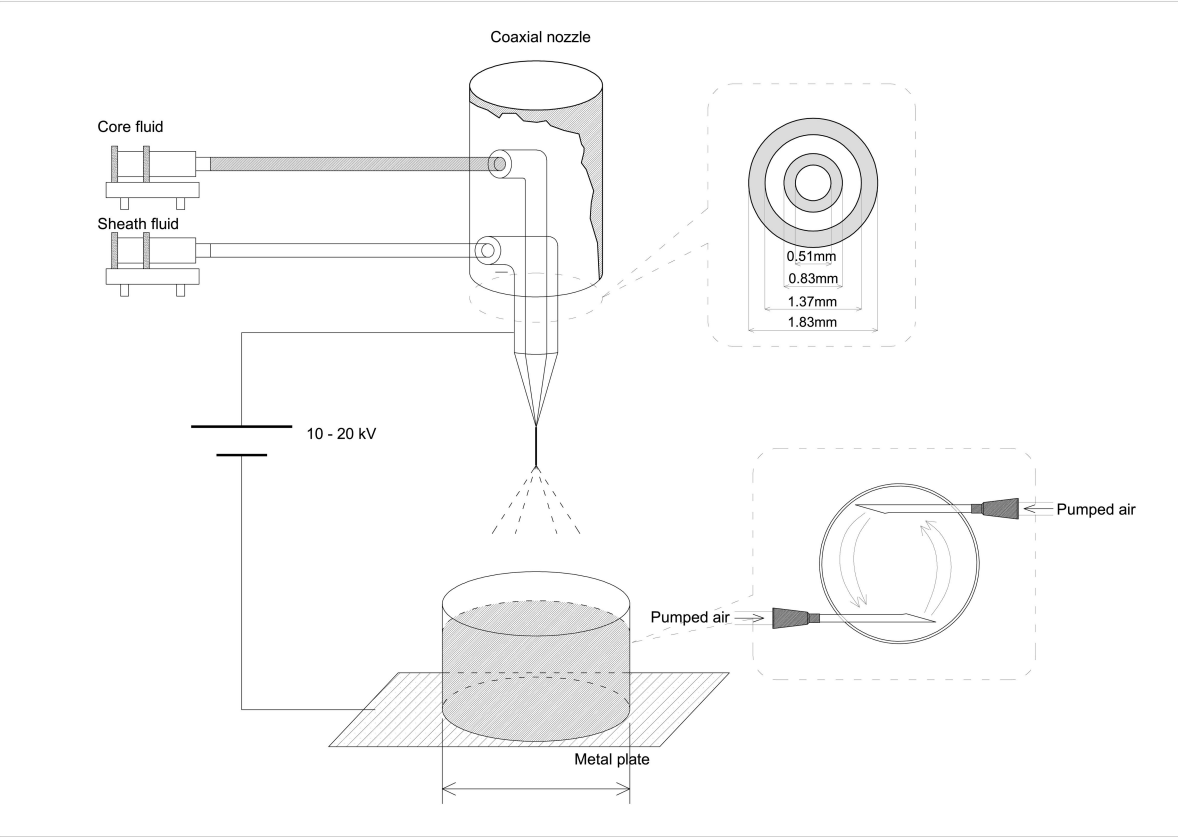

Figure 1. Illustration of the coaxial electrospraying setup

Encapsulation Efficiency Determination

Encapsulation efficiency (EE), the ratio of the mass of DRV effectively enclosed in particles to the total mass of drug available, was determined as follows: 1 ml of the final suspension collected after electrospraying was centrifuged at 14000 rpm and 21°C for 20 min (centrifuge 5804R, Eppendorf, Belgium) after which the sediment was rinsed with 1 ml of 0.1M HCl solution and then dissolved in 100 ml of phosphate buffer at pH 6.8, whereas the supernatant and the above washing solution were filtered

through a PTFE membrane with 0.1µm pore size (Whatman™, GE Healthcare, UK). Drug adsorption to the filter membrane was ruled out in preliminary experiments. The amount of encapsulated DRV dissolved in phosphate buffer as well as the amount of free/non-entrapped DRV in the filtrate was determined by high pressure liquid chromatography (HPLC) analysis using an ODS Hypersil C_{18} reversed phase column (150 x 4.6 mm 5 µm) (Thermo Scientific, USA) connected to a Merk-Hitachi LaChrom system (Merck Darmstadt, Germany). The mobile phase was a mixture of 55:45 (v/v) acetonitrile: 10 mM sodium dihydrogen phosphate buffer (adjusted to pH 4.8 with 1M NaOH) used at a flow rate of 1 ml/min. 20 µl of each samples was injected and the effluent was monitored at 245 nm. The calibration curve was linear in the range of 5 – 200 µM ($R^2 \geq 0.999$). Each sample was analyzed in duplicate. The EE was calculated according to the following equation:

$$EE = \frac{m_{loaded}}{m_{loaded} + m_{free}} x100\%$$

where m_{loaded} is the mass of encapsulated DRV and m_{free} is the mass of the free amount of DRV.

In vitro drug release studies

A weighed amount of the electrosprayed sample was transferred into a glass test tube containing 5 ml of 0.1M HCl solution. The test tube then was rotated at 40 ± 2 rpm using a rotary mixer L26 (Labinco BV, Breda, The Netherlands) at room temperature. After 2 hours, 1 ml of the sample was taken and centrifuged at 14000 rpm for 20 min. The supernatant and the sediment were treated similarly to the process for the encapsulation efficiency test described above. The amount of DRV in the supernatant and in the sediment was then determined by the HPLC method described above. The percentage of drug release was calculated as the ratio of DRV dissolved in the supernatant to the total DRV in the sample. Each sample was analyzed in duplicate.

Particle morphology

The morphology of the encapsulated DRV micro/nanoparticles in initial formulations (particles in collected suspension as such), after lyophilization as well as after dissolution testing in acidic medium was investigated to evaluate the influence of these processes on morphology changes. SEM pictures were recorded using a Phillips XL30 SEM-FEG (Philips, Eindhoven, The Netherlands) equipped with an Schottky field-emission electron gun. A beam of 15 kV was used and detection was performed using a conventional Everhart-Thornley secondary electron detector. The samples were affixed onto an aluminum stub with a double-sided adhesive carbon tape, and then coated with platinum under vacuum using a sputtering device (Balzers Union, Liechtenstein) before imaging.

Particle size distribution

Photon correlation spectroscopy (PCS) was used to investigate the average particle size as well as the particle size distribution (the polydispersity index) of the samples. Light scattering measurements were performed at a fixed angle of 90° on a CGS-3 spectrometer (Malvern Instruments, Worcestershire, UK), equipped with a goniometer, a uniphase 22mV He–Ne laser operating at 632.8nm, an avalanche photodiode detector and an ALV-5000/EPP multiangle tau correlator. Because of the equipment unavailability, for each formulation, only batch 2 was used for PCS measurements.

X-Ray Powder Diffraction (XRPD)

XRPD experiments were carried out at room temperature using an automated X'pert PRO diffractometer (PANalytical, Almelo, the Netherlands) with a Cu X-ray radiation source (K_α radiation, λ=0.1541874 nm). The operating conditions were 45 kV and 40 mA. The electrosprayed sample was placed between two Kapton® polyimide films (Chemplex® Industries Inc., Florida, USA) mounted to a sample holder plate. Measurements were performed in a continuous scan mode from 4° to 35° (2θ) with 0.0167° step size and 200 s counting time.

Results and Discussion

Screening formulation parameters for coaxial electrospraying

In order to tune the processing conditions, screening experiments were performed using single-nozzle electrospraying. A series of core solutions (DRV and HPMC) and shell solutions (different types of enteric polymers) in different solvents or mixture of solvents such as EtOH, DCM, IPA were prepared. The process parameters were adjusted in order to obtain a cone-jet mode operation as stable as possible. A stable cone-jet mode in electrospraying is of utmost importance to generate stable droplets with a mono-disperse size distribution leading to a consistent particle morphology. [15] A single-nozzle was used at first instead of a coaxial nozzle to minimize the complexity of operation of spraying two separated liquids with different physical properties simultaneously. The operating window for stable electrospraying is normally very narrow and is highly dependent on the inter-related properties of the sprayed liquid, the process parameters and the environmental conditions. [16] Thus the preliminary screening with single-nozzle would give an idea how the polymer solutions behave under electrical stress. Firstly, EtOH was selected for dissolving Eudragit L100, and a mixture of DCM: EtOH (50:50) was selected for dissolving HPMCP, HPMCAS and the core solution (DRV and HPMC). However, the cone-jet mode seemed to be unstable at a low concentration of 1% and the solutions dried too quick (jet disappeared at the tip of the nozzle edge). Lowering the applied voltage and/or increasing the polymer concentration (up to 5%) failed to maintain the cone-jet mode. Either the applied voltage was not high enough which resulted in too large droplets or the jet at the tip of the nozzle dried too fast. This could be attributed to the fact that both EtOH and DCM are volatile solvents (boiling temperature of 78.3^0C and 39.6^0C, respectively). Moreover EtOH is practically nonconductive and DCM has a low conductivity of 4.3×10^{-3} μS/m at 20^0C, respectively. Acetone was tried to replace EtOH and the mixture of EtOH: DCM as it is also recommended as a solvent for these polymers but the problem remained unchanged as acetone is also a volatile solvent (boiling point of 56^0C) although it has a significantly higher electrical conductivity (20 μS/m). The fact that the solubility of HPMCP and HPMCAS are limited to a few solvents prevented further investigation using

these polymers at this stage. In case of Eudragit L100, IPA was selected because this solvent has an acceptable electrical conductivity (6 μS/m) and more importantly, higher boiling point temperature (82.6^0C). IPA was also added into the mixture of EtOH and DCM to lower the vapour pressure of this mixture for preparing the core solution. With the presence of IPA, the cone-jet mode was easily obtained for both core and shell solution so in the next stage of the study, the solution of Eudragit L100 in IPA was used as the shell fluid and the solution of DRV with HPMC (weight ratio of 2:1) in a mixture of DCM/EtOH/IPA (2/4/4) was used as the core fluid in coaxial electrospraying.

Preparation of encapsulated DRV nano/microparticles by coaxial electrospraying

In the next series of experiments, the effect of polymer concentration on the spraying process and particles morphology was investigated. Three different concentrations of Eudragit L100 in IPA were tested (1, 3 and 5%). In all experiments, the flow rates of core/shell solution were kept constant (0.5 and 1 ml/hour) but because of the difference in viscosity the applied voltage was slightly adapted (12 – 14 kV) to obtain a stable cone-jet mode. The morphologies of these samples evaluated by SEM are presented in Fig 2. At a concentration of 1%, spherical particles with slightly wrinkled surface were observed. The particle size was uniform and smaller than 1μ. However, this low concentration of Eudragit L100 was not feasible because for a complete coating it required a very low ratio of core and shell flow rate which results in a low productivity/ efficiency. At higher concentration, up to 5%, the similar size of the particles obtained indicated that the concentration had little influence on the size. This could be partly credited to the slightly higher voltage applied for higher polymer concentration solutions. However, some collapsed and bigger particles were observed as well. The collapsed shape of these particles resulted most likely from trapped solvent in the core when they reached the collector. The later evaporation of the trapped solvents made particles collapse at the end. In other words, the shell solidified faster than the core and once the core dried, the particles lost this round shape. The fact this happened at a very high concentration (5%) supports this theory, because in this case more shell or more complete coating is expected, which will hinder the solvent evaporation from the core. Another important observation is that a lot of fibers

were formed, suggesting that the polymer concentration in this case was too high and electrospinning was taking place. During solidification of the droplets, polymer diffusion and/or chain entanglements also play an important role in determining the final morphology of the samples. [10] Chain entanglement obviously depends on polymer concentration and it was previously recommended that for successful electrospraying of particles, the highest possible concentration of polymer should be not larger than three times the critical concentration of overlap for lower molecular weights [17], and even lower for higher molecular weights of the polymer [18]. In case of Eudragit L100 3% solution, SEM analysis showed an acceptable result with less fiber and collapsed particles. The particle size distribution was quite narrow (about 1μm) so this solution was selected for further investigation.

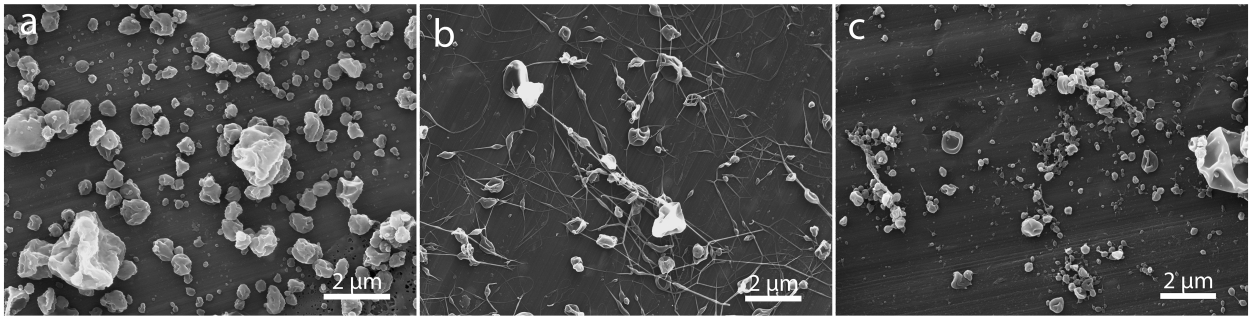

Figure 2. SEM pictures of the formulations using different Eudragit L 100 concentration as shell solution (a) 1%; (b) 5 %; (c) 3%

Particles were, initially, collected on aluminum foil. However the yield was low because the samples were sticking to the aluminum foil. This was due to the fact that the particles were not dry enough or some solvent was still entrapped inside the particles when they were deposited on the collector. Changing the environmental conditions (increase of temperature and/or lower relative humidity) or increase of the distance between the nozzle and the metal collector could certainly be optimized but again this will influence the entire process e.g. field strength, evaporation rate as all the formulation and process parameters have a complex inter-dependence. Therefore, in this pilot study, which had the objective to

demonstrate the feasibility of electrospraying to prepare core-shell solid dispersion particles, we improved the yield by adapting the collector. The particles were collected in an aqueous solution using a homemade conductive cup. However, merely deionized water was not sufficient because the particles were not only very small but also coated with Eudragit L100, a hydrophobic polymer which made them float on the surface of the water. Replacing water with a 1% SLS aqueous solution improved the results as SLS, an anionic surfactant, lowers the interfacial tension and effectively wets the particles. Besides, to facilitate better dispersion of the particles in the solution, air was also pumped through two symmetric needles into the surface of the solution (Fig. 1). SEM pictures show that the particles collected in the solution before and after lyophilization have similar morphology and are comparable to the morphologies of the particles deposited on aluminum foil (Fig. 3).

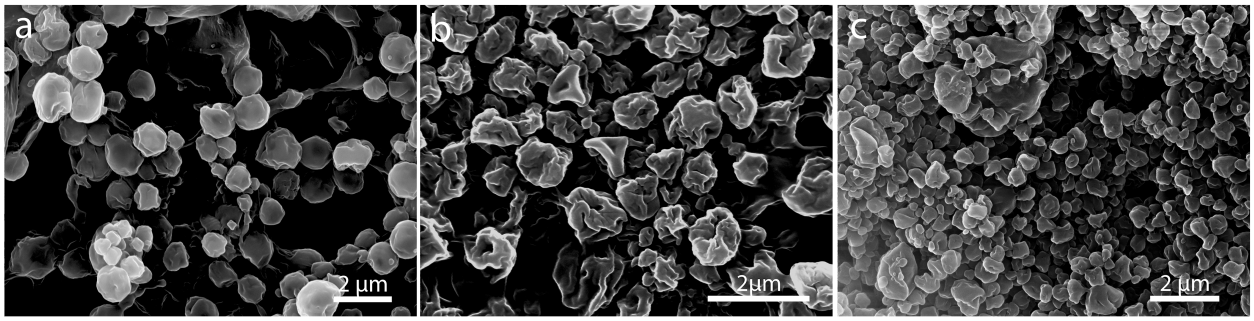

Figure 3. SEM pictures of the formulation F3 (a) collected from 0.1% SLS aqueous solution (b) after lyophilization (c) after dissolution

Influence of the core/shell flow rate on the properties of encapsulated DRV particles prepared by coaxial electrospraying

Five formulations (F1 to F5) with different ratio of core/shell flow rates were prepared. In all experiments, a 3% Eudragit L100 solution in IPA and DRV with HPMC solution in a mixture of DCM/ EtOH/IPA (2/4/4) was used as the shell and core solution, respectively. The applied voltage was slightly changed accordingly to obtain a stable cone-jet spraying mode; other parameters such as distance from the

nozzle to the collector and environmental conditions were kept constant. The details of these formulations are shown in Table 1.

N°	Flow rate (ml/h)		Encapsulation Efficiency (%)		Particle Size (nm)	PDI	Drug release in acidic medium (%)	
	Core	Shell	Batch 1	Batch 2			Batch 1	Batch 2
F1	0.8	1	85.59 (±0.9)	81.97 (±0.8)	1329 ± 290	0.48 ± 0.04	39.98 (±1.9)	45.56 (±2.4)
F2	0.6	0.8	87.53 (±0.8)	84.49 (±0.6)	1396 ± 228	0.37 ± 0.06	36.62 (±2.1)	30.08 (±1.6)
F3	0.8	1.2	87.89 (±1.1)	91.69 (±0.7)	1417 ± 139	0.42 ± 0.05	32.93 (±2.6)	28.77 (±2.3)
F4	0.5	1	89.57 (±0.6)	93.71 (±1.1)	1187 ± 187	0.43 ± 0.05	20.31 (±1.7)	24.39 (±1.9)
F5	0.3	1.2	94.35 (±0.8)	89.77 (±1.4)	1179 ± 99	0.37 ± 0.03	16.77 (±1.1)	19.97 (±1.5)

Table 1. The influence of the ratio of core/shell flow rate on the properties of encapsulated DRV solid dispersion particles prepared by coaxial electrospraying (numbers in paratheses represent range of duplicate measurements). Particle size and PDI results were only collected to Batch 2.

Particle size distribution by DLS

All the samples had more or less similar sizes from 1 to 1.5 µm but as the ratio of core/shell flow rates decreased the size was reduced slightly (Table 1). One could argue that the more shell solution was sprayed the bigger the particles would be as a thicker coating polymer layer was expected. However, one should also take into consideration that the total solid sprayed in all samples was similar and that the initial droplets size, which is influenced by the viscosity of the sprayed fluid and the field strength, have a more important role in determining the size of the final dried particles. The polydispersity indexes of all the samples were in a range of 0.3 to 0.5, which indicated a narrow particle size distribution. It seemed again that decreasing the ratio of core/shell flow rate lowered the polydispersity index, though the difference was negligible. Another interesting observation was that a negligible population of smaller particles of approximately 150 nm appeared in all samples (data not shown). The particle size results determined by DLS were in good agreement with SEM results as some particle fragments were observed surrounding bigger, spherical particles. The subpopulation of smaller particles is most likely resulting

from the Coulomb fission in a small fraction of the electrosprayed droplets before the polymer solidified. [19]

Solid state characterization by XRD

XRD was performed to characterize the amorphism/crystallinity of the drugs in the samples. As observed in Fig . 4, the presence of some distinct Bragg peaks in all samples indicate that a small portion of DRV in the samples was crystalline and not completely amorphous as expected. Incomplete amorphization during electrospraying has been reported previously. [20] However, in that case the model drug was griseofulvin, a very fast crystallizer [21] while DRV is a slower crystallizer. This indicated one probable problem associated to electrospraying as the amorphous drug has to undergo unfavorable conditions such as electrical stress which could induce crystallization. The authors also suggested a solution in form of an instantaneous post-heating of the formulation, but then there was a compromise of changing the surface of the particles. Another interesting observation was that these XRD patterns of the electrosprayed samples were slightly different to the one of crystalline DRV material as some new peaks arose. The original DRV material used for this study was an ethanolate form but it also exists as a hydrate when exposed to moderate or high relativity humidity as ethanol and water in lattice channels can readily exchange with one another. [22] During electrospraying, because of the evaporation of all the solvents, including EtOH, and the presence of water, DRV would crystallize, if anything, into hydrate crystals. However, the emergence of Bragg peaks at 4.5° and 20.4° (2θ) was not observed in the diffractograms of both ethanolate and hydrate crystals of DRV pointing a potential new form of DRV. The polymorphic modification was not further investigated in this study as it was beyond its scope.

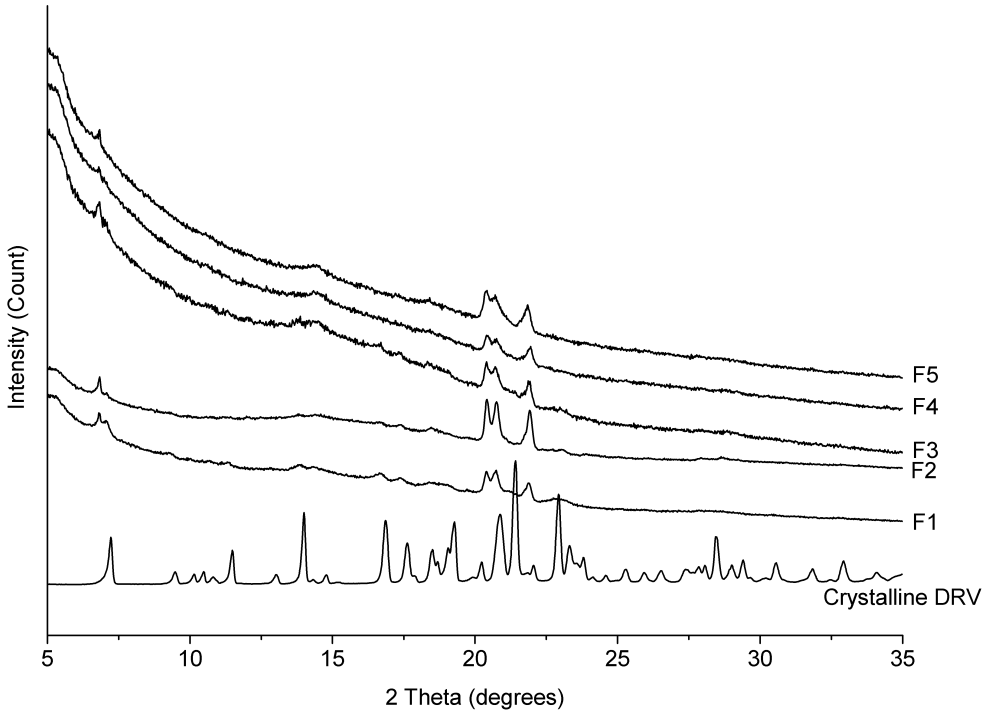

Figure 4. Powder X-Ray diffractogram of encapsulated DRV solid dispersion particles prepared by coaxial electrospraying

Encapsulation Efficiency

As shown in Table 1, the encapsulation efficiency was slightly improved as the ratio of the core/shell flow rates decreased. It was expected because less core solution and more shell solution were sprayed which resulted in more complete coating. However, even in the case of very low core/shell flow rate (0.3/1.2 ml/hr), approximately 90% of DRV was encapsulated into the polymer shell layer. The 10% of free/uncoated DRV could generate a high initial burst release during dissolution. Dialysis can be used to reduce the concentration of free DRV, but in this feasibility study, it was not explored further.

In vitro Dissolution Test

SEM analysis showed that the morphology of particles at the end of the dissolution test was similar to the ones collected after lyophilization (Fig. 3). The percentage of DRV release in acidic medium after 2 hours is shown in Table 1. In all samples, a high initial burst release was observed. The percentage of DRV release reached the maximum value within 10 min, which did not vary till the end of the experiment (2 hours). It was obvious that when the ratio of the core to shell flow rates decreased, DRV was released less in acidic medium because more polymer shell was sprayed compared to core material, leading to a thicker shell layer and more complete coating. The high burst release could be attributed to free/non encapsulated DRV in the samples as revealed in the encapsulation efficiency test as well as the very small particles in the nanosize range. However, when comparing the two formulations F1 and F5 (largest difference in ratio of core/shell flow rates) with just approximately 10% difference in the encapsulation efficiency, the percentage of DRV release decreased considerably from 42% (F1) to 18% (F5). This showed that during the dissolution, DRV at the surface of "flawed" particles and even encapsulated DRV within core-shell structured particles could diffuse through the coating layer into the medium and almost immediately dissolved after that. This emphasizes the importance of a reasonable ratio of core/shell flow rates for a better coating layer, because if one simply keeps decreasing the ratio of core/shell flow rates, the amount of excipient weight fraction in dosage forms would be too high.

Conclusion

In this study, several parameters were investigated to prepare encapsulated DRV solid dispersion nanoparticles using coaxial electrospraying set-up. Provided the right solutions (type of polymer, concentration and solvents) and process variables (applied voltages) were selected, a solid dispersion of DRV was effectively prepared and coated with Eudragit L100 in one single step, though incomplete amorphization was observed by XRD. Encapsulation efficiency testing and in vitro dissolution tests showed that decreasing the ratio of the core/shell flow rates exhibited improvement in encapsulation efficiency and less drug release in acidic medium. This result suggested that coaxial electrospraying is a potential technique for encapsulating solid dispersions within core-shell structured nanoparticles.

However, further studies need to be done for better understanding of the interplay between formulation, process and equipment parameters.

Declarations

The authors declare that they have no conflicts of interest to disclose.

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